Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1-30. (Cancelled)

31. (Withdrawn): A method for removal of contaminating nucleotides from a solution comprising contacting said solution with immobilized DNA complementary to each of the three possibly contaminating nucleotides in the presence of primers and polymerase for a time sufficient to incorporate any contaminating nucleotides into DNA.

32. (Withdrawn): A method for discriminating between the in-phase and out-of-phase sequencing signals comprising:

(i) detecting and measuring error signals thereby determining the size of the trailing strand population;

(ii) between the 3' terminus of the trailing strand primers and the 3' terminus of the leading strand primers;

(iii) simulating the occurrence of an extension failure at a point upstream from the 3' terminus of the leading strands thereby predicting at each extension step the exact point in the sequence previously traversed by the leading strands to which the 3' termini of the trailing strands have been extended

(iv) predicting for each dNTP introduced the signal to be expected from correct extension of the trailing strands; and

(v) subtracting the predicted signal from the measured signal to yield a signal due only to correct extension of the leading strand population.

33. (New): A method of DNA sequencing comprising the steps of:

(a) providing a template system comprising at least one nucleic acid molecule of unknown sequence hybridized to a primer oligonucleotide in the presence of a DNA polymerase with reduce exonuclease activity;

(b) contacting the template system with a single type of deoxyribonucleotide under conditions which allow extension of the primer by incorporation of at least one deoxyribonucleotide having a fluorescent moiety to the 3' end of the primer to form an extended primer;

(c) detecting whether extension of the primer has occurred by detecting a fluorescent signal emitted by the fluorescent moiety, and further comprising destroying the fluorescent signal without removal of the fluorescent moiety;

(d) detecting the number of deoxyribonucleotides incorporated into the primer;

(e) removing unincorporated deoxyribonucleotide; and

(f) repeating steps (a) through (e) to determine the nucleotide sequence of the nucleic acid molecule.

34. (New): The method of claim 33 wherein the fluorescent moiety is destroyed by reaction with compounds capable of extracting an electron from the excited state of the fluorescent moiety.

35. (New): The method of claim 34 wherein the compound is a diphenyliodonium salt.

36. (New): A method of DNA sequencing comprising the steps of:

(a) providing a template system comprising at least one nucleic acid molecule of unknown sequence hybridized to a primer oligonucleotide in the presence of a DNA polymerase with reduced exonuclease activity;

(b) contacting the template system with a single type of deoxyribonucleotide under conditions which allow extension of the primer by incorporation of at least one deoxyribonucleotide to the 3' end of the primer to form an extended primer;

(c) detecting whether extension of the primer has occurred by detecting a change in the concentration of unincorporated deoxyribonucleotide;

(d) detecting the number of deoxyribonucleotides incorporated into the primer;

(e) removing unincorporated deoxyribonucleotide; and

(f) repeating steps (a) through (e) to determine the nucleotide sequence of the nucleic acid molecule.

37. (New): A method of DNA sequencing comprising the steps of:

(a) providing a template system comprising at least one nucleic acid molecule of unknown sequence hybridized to a primer oligonucleotide in the presence of a DNA polymerase with reduced exonuclease activity;

(b) contacting the template system with a single type of deoxyribonucleotide under conditions which allow extension of the primer by incorporation of at least one deoxyribonucleotide having the capability of generating heat to the 3' end of the primer to form an extended primer;

(d) detecting whether extension of the primer has occurred by detecting the heat generated by incorporating the deoxyribonucleotides having the capability to generate heat;

(d) detecting the number of deoxyribonucleotides incorporated into the primer;

(e) removing unincorporated deoxyribonucleotide; and

(f) repeating steps (a) through (e) to determine the nucleotide sequence of the nucleic acid molecule.

38. (New): The method of claim 37 wherein a thermopile is used to detect the generated heat.

39. (New): The method of claim 37 wherein a thermistor is used to detect the generated heat.

40. (New): A method of DNA sequencing comprising the steps of:

(a) providing a template system comprising a buffer and at least one nucleic acid molecule of unknown sequence hybridized to a primer oligonucleotide in the presence of a DNA polymerase with reduced exonuclease activity;

(b) contacting the template system with a single type of deoxyribonucleotide under conditions which allow extension of the primer by incorporation of at least one deoxyribonucleotide which generates heat that is absorbed by the buffer to the 3' end of the primer to form an extended primer;

(c) detecting whether extension of the primer has occurred by measuring the refractive index of the buffer;

(d) detecting the number of deoxyribonucleotides incorporated into the primer;

(e) removing unincorporated deoxyribonucleotide; and

(f) repeating steps (a) through (e) to determine the nucleotide sequence of the nucleic acid molecule.

41. (New): A method of DNA sequencing comprising the steps of:

(a) providing a template system comprising at least one nucleic acid molecule of unknown sequence hybridized to a primer oligonucleotide in the presence of a DNA polymerase with reduced exonuclease activity;

(b) contacting the template system with a single type of deoxyribonucleotide under conditions which allow extension of the primer by incorporation of at least one deoxyribonucleotide to the 3' end of the primer to form an extended primer;

(c) detecting whether extension of the primer has occurred by detecting the concentration of pyrophosphate release by addition of the deoxyribonucleotide to the 3' end of the primer where the concentration of pyrophosphate is detected by hydrolyzing the pyrophosphate and measuring heat generated by hydrolysis of the pyrophosphate;

(d) detecting the number of deoxyribonucleotides incorporated into the primer;

(e) removing unincorporated deoxyribonucleotide; and

(f) repeating steps (a) through (e) to determine the nucleotide sequence of the nucleic acid molecule.

42. (New): A method of DNA sequencing comprising the steps of:

(a) providing a template system comprising at least one nucleic acid molecule of unknown sequence hybridized to a primer oligonucleotide in the presence of a DNA polymerase with reduced exonuclease activity wherein the DNA polymerase is a T4 DNA polymerase with a substitution of amino acid residue Asp112 by Ala and Glu114 by Ala;

(b) contacting the template system with a single type of deoxyribonucleotide under conditions which allow extension of the primer by incorporation of at least one deoxyribonucleotide to the 3' end of the primer to form an extended primer;

(c) detecting whether extension of the primer has occurred;

(d) detecting the number of deoxyribonucleotides incorporated into the primer;

(e) removing unincorporated deoxyribonucleotide; and

(f) repeating steps (a) through (e) to determine the nucleotide sequence of the nucleic acid molecule.

43. (New): The method of claim 40 wherein the DNA polymerase further comprises a T4 DNA polymerase with a substitution of amino acid residue Ile417 by Val.

44. (New): A method of DNA sequencing comprising the steps of:

(a) providing a template system comprising at least one nucleic acid molecule of unknown sequence hybridized to a primer oligonucleotide in the presence of an exonuclease deficient DNA polymerase;

(b) contacting the template system with a single type of deoxyribonucleotide under conditions which allow extension of the primer by incorporation of at least one deoxyribonucleotide having a fluorescent moiety to the 3' end of the primer to form an extended primer;

(c) detecting whether extension of the primer has occurred by detecting a fluorescent signal emitted by the fluorescent moiety and destroying the fluorescent signal without removal of the fluorescent moiety thereby identifying the deoxyribonucleotide added to the 3' end of the primer;

(d) detecting the number of deoxyribonucleotides incorporated into the primer;

(e) removing unincorporated deoxyribonucleotide;

(f) contacting the template system with a mixture including an exonuclease proficient DNA polymerase, an exonuclease deficient DNA polymerase and the identified deoxyribonucleotide of step (b);

(g) removing the mixture of step (f); and

(h) repeating steps (a) through (g) to determine the nucleotide sequence of the nucleic acid molecule.

45. (New): The method of claim 44 wherein the fluorescent moiety is destroyed by reaction with compounds capable of extracting an electron from the excited state of the fluorescent moiety.

46. (New): The method of claim 45 wherein the compound is a diphenyliodonium salt.

47. (New): A method of DNA sequencing comprising the steps of:

(a) providing a template system comprising at least one nucleic acid molecule of unknown sequence hybridized to a primer oligonucleotide in the presence of an exonuclease deficient DNA polymerase;

(b) contacting the template system with a single type of deoxyribonucleotide under conditions which allow extension of the primer by incorporation of at least one deoxyribonucleotide capable of generating heat to the 3' end of the primer to form an extended primer;

(c) detecting whether extension of the primer has occurred by detecting heat generated by incorporating the at least one deoxyribonucleotide thereby identifying the deoxyribonucleotide added to the 3' end of the primer;

(d) detecting the number of deoxyribonucleotides incorporated into the primer;

(e) removing unincorporated deoxyribonucleotide;

(f) contacting the template system with a mixture including an exonuclease proficient DNA polymerase, and exonuclease deficient DNA polymerase and the identified deoxyribonucleotide of step (b);

(g) removing the mixture of step (f); and

(h) repeating steps (a) through (g) to determine the nucleotide sequence of the nucleic acid molecule.

48. (New): The method of claim 47 wherein a thermopile is used to detect the generated heat.

49. (New): The method of claim 47 wherein a thermistor is used to detect the generated heat.

50. (New): A method of DNA sequencing comprising the steps of:

(a) providing a template system comprising a buffer and at least one nucleic acid molecule of unknown sequence hybridized to a primer oligonucleotide in the presence of an exonuclease deficient DNA polymerase;

(b) contacting the template system with a single type of deoxyribonucleotide under conditions which allow extension of the primer by incorporation of at least one deoxyribonucleotide capable of generating heat which is absorbed by the buffer to the 3' end of the primer to form an extended primer;

(c) detecting whether extension of the primer has occurred by measuring the refractive index of the buffer thereby identifying the deoxyribonucleotide added to the 3' end of the primer;

(d) detecting the number of deoxyribonucleotides incorporated into the primer;

(e) removing unincorporated deoxyribonucleotide;

(f) contacting the template system with a mixture including an exonuclease proficient DNA polymerase, an exonuclease deficient DNA polymerase and the identified deoxyribonucleotide of step (b);

(g) removing the mixture of step (f); and

(h) repeating steps (a) through (g) to determine the nucleotide sequence of the nucleic acid molecule.

51. (New): A method of DNA sequencing comprising the steps of:

(a) providing a template system comprising at least one nucleic acid molecule of unknown sequence hybridized to a primer oligonucleotide in the presence of an exonuclease deficient DNA polymerase;

(b) contacting the template system with a single type of deoxyribonucleotide under conditions which allow extension of the primer by

incorporation of at least one deoxyribonucleotide to the 3' end of the primer to form an extended primer;

(c) detecting whether extension of the primer has occurred by detecting the concentration of pyrophosphate released by incorporation of a deoxyribonucleotide to the 3' end of the primer where the concentration of pyrophosphate is detected by hydrolyzing the pyrophosphate and measuring the heat generated by hydrolysis of the pyrophosphate thereby identifying the deoxyribonucleotide added to the 3' end of the primer;

(d) detecting the number of deoxyribonucleotides incorporated into the primer;

(e) removing unincorporated deoxyribonucleotide;

(f) contacting the template system with a mixture including an exonuclease proficient DNA polymerase, an exonuclease deficient DNA polymerase and the identified deoxyribonucleotide of step (b);

(g) removing the mixture of step (f); and

(h) repeating steps (a) through (g) to determine the nucleotide sequence of the nucleic acid molecule.

52. (New): The method of claim 50 wherein the exonuclease deficient DNA polymerase further comprises a T4 DNA polymerase with a substitution of amino acid residue Ile417 by Val.

53. (New): A method of DNA sequencing comprising the steps of:

(a) providing a template system comprising at least one nucleic acid molecule of unknown sequence hybridized to a primer oligonucleotide in the presence of an exonuclease deficient DNA polymerase wherein the exonuclease deficient DNA polymerase is a T4 DNA polymerase with a substitution of amino acid residue Asp112 by Ala and Glu114 by Ala;

(b) contacting the template system with a single type of deoxyribonucleotide under conditions which allow extension of the primer by incorporation of at least one deoxyribonucleotide to the 3' end of the primer to form an extended primer;

(c) detecting whether extension of the primer has occurred thereby identifying the deoxyribonucleotide added to the 3' end of the primer;

(d) detecting the number of deoxyribonucleotides incorporated into the primer;

(e) removing unincorporated deoxyribonucleotide;

(f) contacting the template system with a mixture including an exonuclease proficient DNA polymerase, an exonuclease deficient DNA polymerase and the identified deoxyribonucleotide of step (b);

(g) removing the mixture of step (f); and

(h) repeating steps (a) through (g) to determine the nucleotide sequence of the nucleic acid molecule.